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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,448	09/01/2004	Corrado Fogher	GRT/4161-32	8303

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EXAMINER

WORLEY, CATHY KINGDON

ART UNIT	PAPER NUMBER
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1638

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/506,448	Applicant(s) FOGHER ET AL.	
	Examiner CATHY K. WORLEY	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 February 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 52,53,55-62 and 64-75 is/are pending in the application.
- 4a) Of the above claim(s) 70-75 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 52,53,55-62 and 64-69 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on Feb. 8, 2008, has been entered.

2. The amendment filed Nov. 8, 2007 has been entered.

Claims 1-51, 54, and 63 have been canceled.

Claims 52, 53, 55-62, and 64-75 are pending.

Claims 70-75 are withdrawn because they are not directed to the elected invention.

3. Claims 52, 53, 55-62, and 64-69 are examined in the present office action.

4. This application contains claims 70-75 drawn to an invention nonelected with traverse in the response filed Oct. 23, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Objections and Rejections that are Withdrawn

5. The objections to claims 52, 61, and 68 are withdrawn in light of the Applicant's amendments to the claims.
6. The rejections of claims 59, 63, and 68 under 35 USC 112, second paragraph are withdrawn in light of the Applicant's amendments to the claims.
7. The rejections of claims 52-69 under 35 USC 112, first paragraph for lack of written description and enablement are withdrawn in light of the Applicant's amendments to the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 52, 53, 55-62, and 64-69 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Radin et al. (US Patent No. 5,929,304, issued on Jul. 27, 1999) in view of Watanabe (GenBank Accession D16107, published on Feb. 1, 2000),

further in view of Fogher (WO 00/04146, published on Jan. 27, 2000), and further in view of Whitelam GC (J. Sci. Food Agric. (1995) Vol. 68, pp. 1-9). The Applicant's arguments in the response filed on Nov. 8, 2007, were fully considered, but were not found to be persuasive.

The claims are drawn to a transformed plant that comprises an expression vector comprising the promoter of SEQ ID NO:6 (which is the promoter from the soybean basic 7S globulin gene), the signal sequence of SEQ ID NO:7 which is able to target an enzyme to seed storage organs and to provide the post-translational modifications required for enzymatic activity, and a sequence encoding a lysosomal enzyme.

Radin et al teach plants transformed with a recombinant expression construct encoding a lysosomal enzyme (see claim 33). They teach the production of enzymatically active recombinant lysosomal enzymes of both human and animal origin (see abstract). They teach the use of several different signal peptides (see column 14, lines 31-67 and column 15, lines 1-9). They teach the removal of the signal peptide (see column 14, lines 33). They teach expression vectors that are plasmids (see column 22, line 1). Rabin et al teach plants expressing any one of a list of lysosomal enzymes (see claims 26, 27, 47, and 48), and this list includes glucocerebrosidase, which is recited in the instant claims and reduced to practice in the instant application. They specifically teach transgenic tobacco plants

expressing a lysosomal enzyme (see columns 21-25). They teach a seed of such a plant (see claims 54-57).

Radin et al do not teach a promoter of SEQ ID NO:6, nor do they teach expression in an amount of at least 0.8% of seed extracted total proteins, nor do they teach a signal sequence of SEQ ID NO:7.

Watanabe teaches the soybean basic 7S globulin promoter that comprises SEQ ID NO:6 (see sequence alignment).

Fogher teaches the signal sequence encoded by SEQ ID NO:7 (see sequence alignment). Fogher teaches that expression cassettes were made with regulation elements from the 7S basic globulin gene (see second paragraph on page 23, and entire document). Fogher teaches that yields of 1% to 1.8% of seed total storage proteins were achieved for a recombinant protein expressed utilizing these regulatory elements (see first paragraph on page 22).

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to modify the plants taught by Radin et al to substitute the soybean basic 7S globulin promoter and signal sequence for the promoters and signal peptides taught by Radin et al.

In the prior art, Radin et al teach plants, seeds, and methods that differ from the instant invention only by the promoter and signal sequences utilized.

At the time the invention was made, the promoter from the soybean 7S globulin gene (SEQ ID NO:6) and the nucleic acid sequence encoding the signal

peptide (SEQ ID NO:7) were known in the art (taught by Watanabe and Fogher, respectively). Their functions as a seed-preferred promoter and as a signal sequence capable of targeting proteins through the secretory pathway to yield properly glycosylated recombinant proteins were known in the art (see Fogher: paragraph bridging pages 19-20, and page 21, and paragraph bridging pages 29-30).

At the time the invention was made, one of ordinary skill could have substituted the promoter sequence taught by Watanabe and the signal sequence taught by Fogher for the regulatory elements utilized by Radin et al. One of ordinary skill would have predicted producing a higher yield of recombinant protein in the seeds of the resulting transgenic plant, based on the teachings of Fogher et al (see first paragraph on page 22).

One of ordinary skill in the art would have had additional motivation for this design choice because Whitelam teaches that expression of valuable recombinant enzymes in seeds is desirable because the recombinant enzymes can be stored for long periods in dry seeds (see page 8, second paragraph). Whitelam discusses “bio-farming” in general (see abstract and page 2, second paragraph), and specifically teaches that there are advantages to seed-localized expression of recombinant proteins (see page 2, right column).

Given the successes and advantages of expressing recombinant enzymes in seeds, taught by Whitelam, one would have expected to succeed in expressing the lysosomal enzymes taught by Radin in seeds. Given the success of Fogher in

expressing a recombinant protein utilizing regulatory elements from the soybean basic 7S globulin gene, one would have had an expectation of success in utilizing SEQ ID NOs: 6 and 7 as regulatory elements.

The Applicant argues that there would not have been a reasonable expectation of success to use seeds as an effective and stable storage organ for enzymes because Radin discloses that glucocerebrosidase was not stable in leaf, stem, flower, and fruit (see last paragraph on page 11 of the response).

This is not persuasive, however, because Radin does not teach that expression in seeds is unstable, and Whitelam teaches that seeds are a favored site for recombinant protein accumulation in plants (see right column on page 2). Whitelam specifically teaches that recombinant enzymes can be stored for long periods of time in dry seeds (see second paragraph in left column on page 8). Therefore, one of ordinary skill in the art would have expected the recombinant lysosomal enzymes to be more stable in dry seeds than in other plant tissues, and there would have been a reasonable expectation of success in combining the cited references.

The Applicant argues that one would not have found a reasonable expectation of success in using the 7S promoter to expression a lysosomal enzyme because there is no indication in the prior art that the enzyme could be purified in active form from seeds (see first paragraph on page 12 of the response).

This is not persuasive, however, because Whitelam teaches recombinant therapeutic proteins and enzymes can be produced by bio-farming (see entire article). Furthermore, Whitelam specifically teaches that recombinant enzymes can be stored for long periods of time in dry seeds (see second paragraph in left column on page 8). Therefore, one of ordinary skill in the art would have expected that recombinant lysosomal enzymes could also be produced in and purified from seeds.

The Applicant argues that although Whitelam discloses that expression of recombinant enzymes in seeds would be desirable, the cited documents leave open the problems solved by the present invention (see second paragraph on page 12 of the response).

This is not persuasive, because the only problem known in the prior art was instability of one particular lysosomal enzyme in leaf, stem, flower, and fruit. The problem can be overcome by expressing the enzyme in seeds, which were known in the prior art to be desirable for the accumulation and stable storage of recombinant enzymes. Therefore, the combination of references cited by the Examiner overcomes problems in the prior art and renders the instant invention obvious.

9. No claims are allowed.

10. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally

rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CKW/

/Anne R. Kubelik/
Primary Examiner, Art Unit 1638